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NEWS	3	JAN 16	CA/CAplus Company Name Thesaurus enhanced and reloaded
NEWS	4	JAN 16	IPC version 2007.01 thesaurus available on STN
NEWS	5	JAN 16	WPIDS/WPINDEX/WPIX enhanced with IPC 8 reclassification data
NEWS	6	JAN 22	CA/CAplus updated with revised CAS roles
NEWS	7	JAN 22	CA/CAplus enhanced with patent applications from India
NEWS	8	JAN 29	PHAR reloaded with new search and display fields
NEWS	9	JAN 29	CAS Registry Number crossover limit increased to 300,000 in multiple databases
NEWS	10	FEB 15	PATDPASPC enhanced with Drug Approval numbers
NEWS	11	FEB 15	RUSSIAPAT enhanced with pre-1994 records
NEWS	12	FEB 23	KOREAPAT enhanced with IPC 8 features and functionality
NEWS	13	FEB 26	MEDLINE reloaded with enhancements
NEWS	14	FEB 26	EMBASE enhanced with Clinical Trial Number field
NEWS	15	FEB 26	TOXCENTER enhanced with reloaded MEDLINE
NEWS	16	FEB 26	IFICDB/IFIPAT/IFIUDB reloaded with enhancements
NEWS	17	FEB 26	CAS Registry Number crossover limit increased from 10,000 to 300,000 in multiple databases
NEWS	18	MAR 15	WPIDS/WPIX enhanced with new FRAGHITSTR display format
NEWS	19	MAR 16	CASREACT coverage extended
NEWS	20	MAR 20	MARPAT now updated daily
NEWS	21	MAR 22	LWPI reloaded
NEWS	22	MAR 30	RDISCLOSURE reloaded with enhancements
NEWS	23	APR 02	JICST-EPLUS removed from database clusters and STN
NEWS	24	APR 30	GENBANK reloaded and enhanced with Genome Project ID field
NEWS	25	APR 30	CHEMCATS enhanced with 1.2 million new records
NEWS	26	APR 30	CA/CAplus enhanced with 1870-1889 U.S. patent records
NEWS	27	APR 30	INPADOC replaced by INPADOCDB on STN
NEWS	28	MAY 01	New CAS web site launched
NEWS	29	MAY 08	CA/CAplus Indian patent publication number format defined

NEWS EXPRESS	NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8

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FILE COVERS 1907 - 9 May 2007 VOL 146 ISS 20
FILE LAST UPDATED: 8 May 2007 (20070508/ED)

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http://www.cas.org/infopolicy.html

```
=> s dipeptidyl peptidase IV
          4567 DIPEPTIDYL
         13618 PEPTIDASE
          4804 PEPTIDASES
         15808 PEPTIDASE
                 (PEPTIDASE OR PEPTIDASES)
        527396 IV
           993 IVS
        528290 IV
                 (IV OR IVS)
L1         2176 DIPEPTIDYL PEPTIDASE IV
                 (DIPEPTIDYL(W)PEPTIDASE(W)IV)

=> s l1 and inhibitor?
       1037659 INHIBITOR?
L2        1037 L1 AND INHIBITOR?

=> s l2 and diabetes
        124542 DIABETES
L3         541 L2 AND DIABETES

=> s l3 and py<2002
      21897254 PY<2002
L4           45 L3 AND PY<2002

=> d ibib abs hitstr 1-10

L4   ANSWER 1 OF 45  CAPLUS  COPYRIGHT 2007 ACS on STN
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ACCESSION NUMBER: 2006:95030 CAPLUS
DOCUMENT NUMBER: 144:177472
TITLE: Controlled release α-lipoic acid formulation with an inositol compound
INVENTOR(S): Byrd, Edward A.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 26 pp., Cont.-in-part of U.S. Ser. No. 412,559.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006024367	A1	20060202	US 2005-199919	20050808
US 6197340	B1	20010306	US 1999-288245	19990408 <--
US 2001028896	A1	20011011	US 2001-755890	20010105 <--
US 6572888	B2	20030603		
US 2003228362	A1	20031211	US 2003-412559	20030411
US 7118762	B2	20061010		
WO 2007019540	A2	20070215	WO 2006-US30984	20060808

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.:

US 1998-87203P	P	19980528
US 1998-112623	B2	19980709
US 1998-102605P	P	19981001
US 1999-288245	A2	19990408
US 2001-755890	A1	20010105
US 2003-412559	A2	20030411
US 2005-199919	A	20050808

AB A biphasic formulation of an inositol compound and lipoic acid for oral administration is disclosed. The lipoic acid and the inositol compound are combined with excipient materials in such a way that those materials provide for an immediate release of a first portion of the active ingredients from the formulation followed by a gradual release of any remaining active ingredients in a manner which makes it possible to (1) quickly obtain a therapeutic level of the active ingredients; and (2) substantially increase the period of time over which therapeutic levels of the active ingredients are maintained relative to a quick release formulation. These features make it possible to use the formulation to reduce serum glucose levels and maintain those reduced glucose levels over time to treat diabetic polyneuropathy and thereby obtaining a range of desired therapeutic results.

L4 ANSWER 2 OF 45 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1292022 CAPLUS
DOCUMENT NUMBER: 144:45722
TITLE: GIP peptide analogs resistant to degradation by DPP IV for treatment of diabetes, insulin resistance and obesity
INVENTOR(S): Gault, Victor A.; O'Harte, Finbarr Paul Mary; Irwin,

Nigel; Harriott, Patrick; Flatt, Peter Raymond
PATENT ASSIGNEE(S): Ire.
SOURCE: U.S. Pat. Appl. Publ., 87 pp., Cont.-in-part of Appl. No. PCT/GB05/000710.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005272652	A1	20051208	US 2005-90787	20050325
WO 2000058360	A2	20001005	WO 2000-GB1089	20000329 <--
WO 2000058360	A3	20010125		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 6921748	B1	20050726	US 2002-937687	20020108
WO 2005082928	A2	20050909	WO 2005-GB710	20050225
WO 2005082928	A3	20051201		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:		
GB 1999-7216	A	19990329
GB 1999-17565	A	19990727
WO 2000-GB1089	W	20000329
US 2002-937687	A2	20020108
GB 2004-4124	A	20040225
WO 2005-GB710	A2	20050225

AB The present invention provides peptide analogs which are antagonists of gastric inhibitory peptide (GIP). The peptides, based on GIP 1-42 include substitutions and/or modifications which have enhanced resistance to degradation by the enzyme dipeptidyl peptidase IV (DPP IV). The invention also provides a process of N terminally modifying GIP and the use of the peptide analogs for treatment of diabetes.

L4 ANSWER 3 OF 45 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:737359 CAPLUS
DOCUMENT NUMBER: 139:240366
TITLE: Dipeptidyl peptidase IV inhibitors and their uses for lowering blood pressure levels
INVENTOR(S): Pospisilik, Andrew J.; Demuth, Hans-Ulrich; Glund, Konrad; Hoffmann, Matthias; McIntosh, Christopher H. S.; Pederson, Ray A.
PATENT ASSIGNEE(S): Can.
SOURCE: U.S. Pat. Appl. Publ., 38 pp., Cont.-in-part of U. S. Ser. No. 932,546.

CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003176357	A1	20030918	US 2002-200919	20020723
US 6303661	B1	20011016	US 1998-155833	19981006 <--
US 2002006899	A1	20020117	US 2001-932546	20010817
US 2005107308	A1	20050519	US 2004-970526	20041021

PRIORITY APPLN. INFO.:	US 1998-155833	A2	19981006
	US 2001-932546	A2	20010817
	DE 1996-19616486	A	19960425
	WO 1997-DE820	W	19970424
	US 2002-200919	A1	20020723

OTHER SOURCE(S): MARPAT 139:240366

AB The invention provides new uses of DPIV-inhibitors of the invention, and their corresponding pharmaceutically acceptable acid addition salt forms, for lowering blood pressure levels. Compds. of the invention include peptides and peptide-like compds. (preparation described).

L4 ANSWER 4 OF 45 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:492685 CAPLUS
DOCUMENT NUMBER: 139:47176
TITLE: Methods for improving islet signaling in diabetes mellitus and obesity using dipeptidyl peptidase IV inhibitors
INVENTOR(S): Demuth, Hans-Ulrich; Glund, Konrad; Pospisilik, J. Andrew; Kuehn-Wache, Kerstin
PATENT ASSIGNEE(S): Prosidion Limited, Germany
SOURCE: U.S. Pat. Appl. Publ., 41 pp., Cont.-in-part of U.S. Ser. No. 824,622.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003119736	A1	20030626	US 2002-216349	20020809
US 6890905	B2	20050510		
US 2001051646	A1	20011213	US 2001-824622	20010402 <--
US 6500804	B2	20021231		
US 2002198242	A1	20021226	US 2002-196038	20020716
US 2003008905	A1	20030109	US 2002-200870	20020722
WO 2004017989	A1	20040304	WO 2002-EP8931	20020809
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
AU 2002331226	A1	20040311	AU 2002-331226	20020809
EP 1528931	A1	20050511	EP 2002-767358	20020809
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IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK

US 2005222221	A1	20051006	US 2003-676832	20031001
US 2005014703	A1	20050120	US 2004-910176	20040802
PRIORITY APPLN. INFO.:			US 2001-824622	A2 20010402
			US 2000-194061P	P 20000331
			US 2002-196038	A1 20020716
			US 2002-200870	A1 20020722
			WO 2002-EP8931	A 20020809

AB The present invention discloses methods for therapeutically treating mammals, including but not limited to humans, to increase the relative insulin producing performance of endogenous pancreatic β-cells, to cause differentiation of pancreatic epithelial cells into insulin producing β-cells, to improve muscle sensitivity to insulin and other weight control efforts by the chronic oral administration of a dipeptidyl peptidase (DP IV) inhibitor. The administration causes the active form of GLP-1 and other non-nutrient stimulated growth hormones to remain biol. active longer under physiol. conditions. The extended presence of such hormones, in particular in the pancreatic tissue can also facilitate differentiation and regeneration of the β-cells already present that are in need of repair.

REFERENCE COUNT: 114 THERE ARE 114 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 45 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:935405 CAPLUS
DOCUMENT NUMBER: 136:48456
TITLE: Combinations of depeptidyl peptidase IV inhibitors and other antidiabetic agents for the treatment of diabetes mellitus
INVENTOR(S): Arch, Jonathan Robert Sanders; Lenhard, James Martin
PATENT ASSIGNEE(S): Smithkline Beecham PLC, UK; Smithkline Beecham Corporation
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001097808	A1	20011227	WO 2001-GB2696	20010619 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2413299	A1	20011227	CA 2001-2413299	20010619 <--
EP 1292300	A1	20030319	EP 2001-938472	20010619
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001011800	A	20030527	BR 2001-11800	20010619
HU 200301194	A2	20030828	HU 2003-1194	20010619
JP 2003535898	T	20031202	JP 2002-503292	20010619
BG 107385	A	20030930	BG 2002-107385	20021212
NO 2002006038	A	20030203	NO 2002-6038	20021216
IN 2002MN01834	A	20050204	IN 2002-MN1834	20021218
ZA 2003000203	A	20040326	ZA 2003-203	20030108

US 2003166578	A1	20030904	US 2003-311446		20030220
US 7078397	B2	20060718			
AU 2005232303	A1	20051201	AU 2005-232303		20051111
US 2006205675	A1	20060914	US 2006-421548		20060601
PRIORITY APPLN. INFO.:			GB 2000-14969	A	20000619
			AU 2001-64148	A3	20010619
			WO 2001-GB2696	W	20010619
			US 2003-311446	A1	20030220

AB A method for the treatment of diabetes mellitus, especially Type 2 diabetes and conditions associated with diabetes mellitus in a mammal, e.g. a human, comprises administering an effective, nontoxic and pharmaceutically acceptable amount of a dipeptidyl peptidase IV inhibitor and another antidiabetic agent to a mammal in need thereof.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 45 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:923757 CAPLUS
DOCUMENT NUMBER: 136:37503
TITLE: Preparation of N-glycyl-2-cyanopyrrolidines as DPP IV inhibitors
INVENTOR(S): Villhauer, Edwin Bernard
PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis-Erfindungen Verwaltungsgesellschaft m.b.H.
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2001096295	A2	20011220	WO 2001-EP6595		20010611 <--
WO 2001096295	A3	20020516			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
TW 583185	B	20040411	TW 2001-90113972		20010608
CA 2411778	A1	20011220	CA 2001-2411778		20010611 <--
EP 1296974	A2	20030402	EP 2001-984014		20010611
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JP 2004503531	T	20040205	JP 2002-510439		20010611
US 6432969	B1	20020813	US 2001-879654		20010612
US 2002193390	A1	20021219	US 2002-176440		20020620
PRIORITY APPLN. INFO.:			US 2000-325743P	P	20000613
			US 2000-592336	A	20000613
			WO 2001-EP6595	W	20010611
			US 2001-879654	A3	20010612

OTHER SOURCE(S): MARPAT 136:37503

AB The present invention relates to the preparation of N-(substituted glycyl)-2-cyanopyrrolidines. Thus, 1-chloroacetyl-2-(S)-cyanopyrrolidine (synthetic preparation given) is reacted with 2-[(5-chloro-2-pyridinyl)amino]-1,1-dimethylethylamine in the presence of K2CO3 to give 1-[[[2-[(5-chloro-2-pyridinyl)amino]-1,1-dimethylethyl]amino]acetyl]-2-

cyano-(S)-pyrrolidine. The prepared compds. inhibit DPP-IV (dipeptidyl-peptidase-IV) activity. They are therefore indicated for use as pharmaceuticals in inhibiting DPP-IV and in the treatment of conditions mediated by DPP-IV, such as non-insulin-dependent diabetes mellitus, arthritis, obesity, osteoporosis and further conditions of impaired glucose tolerance. Data for biol. activity of some of the prepared compds. were given.

L4 ANSWER 7 OF 45 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:880555 CAPLUS
DOCUMENT NUMBER: 136:160751
TITLE: P32/98: Antidiabetic dipeptidyl-peptidase IV inhibitor
AUTHOR(S): Sorbera, L. A.; Revel, L.; Castaner, J.
CORPORATE SOURCE: Prous Science, Barcelona, 08080, Spain
SOURCE: Drugs of the Future (2001), 26(9), 859-864
CODEN: DRFUD4; ISSN: 0377-8282
PUBLISHER: Prous Science
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review discusses the synthesis, pharmacol. actions, and clin. studies of P32/98, a novel class of antidiabetic agents. P32/98 is a highly specific, reversible, competitive, transition-state analog inhibitor of the regulatory enzyme, dipeptidyl peptidase IV that is involved in signal transduction processes occurring during the immune responses leading to development of type 2 diabetes. It has been chosen for further development as an agent having the potential to improve glucose tolerance and thus be advantageous in the management of type 2 diabetes.

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 45 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:868260 CAPLUS
DOCUMENT NUMBER: 136:627
TITLE: Combinations of enzyme inhibitor-containing preparations and the use in inhibition of mononuclear cells and T-cells and treatment of immune conditions
INVENTOR(S): Ansorge, Siegfried; Arndt, Marco; Buehling, Frank; Lendeckel, Uwe; Neubert, Klaus; Reinhold, Dirk
PATENT ASSIGNEE(S): Institut fuer Medizintechnologie Magdeburg G.m.b.H. IMTM, Germany
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001089569	A1	20011129	WO 2001-EP5887	20010522 <--
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 10025464	A1	20011206	DE 2000-10025464	20000523 <--
CA 2410305	A1	20021122	CA 2001-2410305	20010522

EP 1289559	A1	20030312	EP 2001-945184		20010522
EP 1289559	B1	20050727			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
JP 2003534293	T	20031118	JP 2001-585811		20010522
AU 2001267475	B2	20041104	AU 2001-267475		20010522
AT 300313	T	20050815	AT 2001-945184		20010522
ES 2243516	T3	20051201	ES 2001-1945184		20010522
US 2005014699	A1	20050120	US 2004-296102		20040326
PRIORITY APPLN. INFO.:			DE 2000-10025464	A	20000523
			WO 2001-EP5887	W	20010522

AB A method is disclosed which permits, owing to the simultaneous and joint inhibition of the enzyme activities of (1) alanyl-aminopeptidase and dipeptidyl-peptidase IV, (2) dipeptidyl-peptidase IV and angiotensin-converting enzyme, (3) dipeptidyl-peptidase IV and prolyl-oligopeptidase, and (4) dipeptidyl-peptidase IV and X-Pro-aminopeptidase, the inhibition of DNA synthesis and thus the proliferation of mononuclear cells and T cells to an extent which cannot be obtained by individual application of the enzyme inhibitors, even when used in higher doses. Although the above-mentioned inhibitors influence the same process, namely DNA synthesis and thus the proliferation of immune cells, this effect is not complete and not long-lasting when the inhibitors are used individually. The functional overlapping of enzymic activities results, as is supported by exptl. data, in an additive/superadditive inhibitory effect on DNA synthesis and the proliferation resulting from the simultaneous inhibition of a plurality of the above enzymes. The invention shows that the simultaneous application of inhibitors of the above enzymes or of corresponding prepns. and forms of administration is suitable for the therapy of autoimmune diseases and chronic diseases with an inflammatory genesis, as well as for the treatment of post-transplant rejection episodes.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 45 CAPLUS COPYRIGHT 2007 ACS on STN

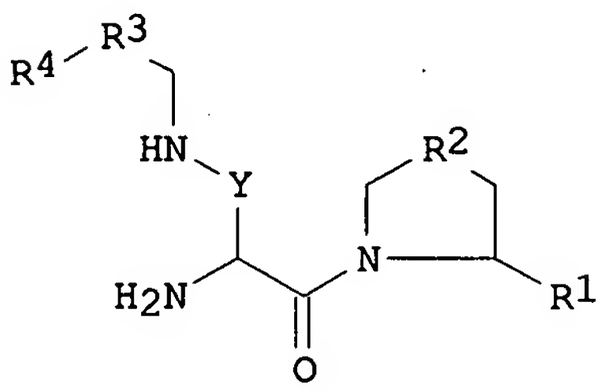
ACCESSION NUMBER: 2001:798217 CAPLUS
DOCUMENT NUMBER: 135:344736
TITLE: preparation of peptidomimetics as inhibitors of dipeptidyl peptidase IV
INVENTOR(S): Evans, David Michael; Pitt, Gary Robert William
PATENT ASSIGNEE(S): Ferring B.V., Neth.
SOURCE: PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001081337	A1	20011101	WO 2001-GB1875	20010426 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2407662	A1	20011101	CA 2001-2407662	20010426 <--

BR 2001010021	A	20030121	BR 2001-10021		20010426
EP 1280797	A1	20030205	EP 2001-923854		20010426
EP 1280797	B1	20041013			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
HU 200300563	A2	20030728	HU 2003-563		20010426
HU 200300563	A3	20061128			
NZ 522436	A	20030926	NZ 2001-522436		20010426
JP 2003531204	T	20031021	JP 2001-578427		20010426
EE 200200603	A	20040415	EE 2002-603		20010426
AT 279408	T	20041015	AT 2001-923854		20010426
PT 1280797	T	20050131	PT 2001-923854		20010426
ES 2231474	T3	20050516	ES 2001-1923854		20010426
AU 784007	B2	20060112	AU 2001-50537		20010426
RU 2280035	C2	20060720	RU 2002-131639		20010426
IN 2002DN00992	A	20050128	IN 2002-DN992		20021004
HR 2002000813	B1	20060228	HR 2002-813		20021010
ZA 2002008523	A	20030825	ZA 2002-8523		20021022
NO 2002005118	A	20021024	NO 2002-5118		20021024
US 2004082497	A1	20040429	US 2003-258804		20030117
US 7125863	B2	20061024			
HK 1051043	A1	20050513	HK 2003-103249		20030507
PRIORITY APPLN. INFO.:			GB 2000-10188	A	20000426
			WO 2001-GB1875	W	20010426

OTHER SOURCE(S): MARPAT 135:344736

GI



I

AB Compds. of formula I [R1 = H or CN; R2 = S, O, SO2 or CH2; R3 = CO, CH2 or covalent bond; R4 = optionally substituted aromatic N-containing heterocycle; Y = (CH2)n; n = 1-5] were prepared as inhibitors of dipeptidyl peptidase IV. Thus, compound I (R1 = CN, R2 = H, R3 = CO, R4 = pyrazine, n = 3) was prepared as trifluoroacetate via coupling of (2S)-pyrrolidine-2-carbonitrile hydrochloride (preparation given) with Nα-BOC-Nw-pyrazinyl-2-carbonyl-L-ornithine(BOC = tert-butoxycarbonyl). Compds. of the invention were competitive inhibitors of dipeptidyl peptidase IV with Ki values less than 300 nM.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 45 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:730537 CAPLUS

DOCUMENT NUMBER: 135:267253

TITLE: Method using dipeptidyl peptidase IV (DPIV) inhibitors for the improvement of islet signaling in diabetes mellitus and for its prevention

INVENTOR(S): Demuth, Hans-Ulrich; Glund, Konrad
PATENT ASSIGNEE(S): Probiodrug Gesellschaft Fuer Arzneimittelforschung MBH, Germany
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001072290	A2	20011004	WO 2001-EP3725	20010402 <--
WO 2001072290	A3	20020314		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2400226	A1	20011004	CA 2001-2400226	20010402 <--
CA 2400226	C	20070102		
AU 200154763	A	20011008	AU 2001-54763	20010402 <--
EP 1283735	A2	20030219	EP 2001-927848	20010402
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HU 200204459	A2	20030528	HU 2002-4459	20010402
BR 2001009553	A	20030603	BR 2001-9553	20010402
JP 2003528135	T	20030924	JP 2001-570251	20010402
RU 2261096	C2	20050927	RU 2002-129014	20010402
US 2002198242	A1	20021226	US 2002-196038	20020716
US 2003008905	A1	20030109	US 2002-200870	20020722
IN 2002MN01089	A	20050304	IN 2002-MN1089	20020807
AU 2002331226	A1	20040311	AU 2002-331226	20020809
EP 1528931	A1	20050511	EP 2002-767358	20020809
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
ZA 2002006460	A	20030813	ZA 2002-6460	20020813
NO 2002004643	A	20021105	NO 2002-4643	20020927
US 2005222221	A1	20051006	US 2003-676832	20031001
US 2005014703	A1	20050120	US 2004-910176	20040802
AU 2006202344	A1	20060622	AU 2006-202344	20060601

PRIORITY APPLN. INFO.:

US 2000-194061P	P	20000331
AU 2001-254763	A3	20010402
US 2001-824622	A3	20010402
WO 2001-EP3725	W	20010402
US 2002-196038	A1	20020716
US 2002-200870	A1	20020722
WO 2002-EP8931	A	20020809

AB The invention discloses a method for therapeutically treating mammals, including but not limited to humans, to increase the relative insulin-producing performance of endogenous pancreatic β-cells and to cause differentiation of pancreatic epithelial cells into insulin-producing β-cells. Oral administration of a DPIV inhibitor causes the active form of GLP-1 to be preserved longer under physiol. conditions. The extended presence of GLP-1, in particular in the pancreatic tissue facilitates differentiation and regeneration of the β-cells already present that are in need of repair. These repaired insulin-producing cells can contribute to the correction and maintenance of normal physiol. glycemic levels.

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=> d ibib abs hitstr 11-20

L4   ANSWER 11 OF 45  CAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2001:693281  CAPLUS
DOCUMENT NUMBER:          135:257147
TITLE:                    Preparation of fused cyclopropylpyrrolidine-based
                          inhibitors of dipeptidyl
                          peptidase IV
INVENTOR(S):              Robl, Jeffrey A.; Sulsky, Richard B.; Augeri, David
                          J.; Magnin, David R.; Hamann, Lawrence G.; Betebenner,
                          David A.
PATENT ASSIGNEE(S):       Bristol-Myers Squibb Co., USA
SOURCE:                   PCT Int. Appl., 135 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

PATENT NO.              KIND   DATE        APPLICATION NO.              DATE
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WO 2001068603           A2     20010920    WO 2001-US7151               20010305 <--
WO 2001068603           A3     20020214
    W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR,
        CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU,
        ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU,
        LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE,
        SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW
    RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
        DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
        BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
US 2002019411           A1     20020214    US 2001-788173               20010216
US 6395767              B2     20020528
CA 2402894              A1     20010920    CA 2001-2402894              20010305 <--
EP 1261586              A2     20021204    EP 2001-918383               20010305
    R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
        IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
JP 2003531118           T      20031021    JP 2001-567699               20010305
HU 200302792            A2     20031229    HU 2003-2792                 20010305
BR 2001009115           A      20031230    BR 2001-9115                 20010305
NZ 520821               A      20041126    NZ 2001-520821               20010305
EP 1559710              A2     20050803    EP 2005-5368                 20010305
    R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
        IE, FI, CY, TR
    CN 1698601          A      20051123    CN 2005-10078518             20010305
    TW 258468           B      20060721    TW 2001-90104965             20010305
    RU 2286986          C2     20061110    RU 2002-125491               20010305
    IN 2002MN01154      A      20050304    IN 2002-MN1154               20020823
    ZA 2002006816       A      20031126    ZA 2002-6816                 20020826
    NO 2002004295       A      20021106    NO 2002-4295                 20020909
PRIORITY APPLN. INFO.:                      US 2000-188555P      P       20000310
                                            CN 2001-806315       A3      20010305
                                            EP 2001-918383       A3      20010305
                                            WO 2001-US7151       W       20010305

OTHER SOURCE(S):          MARPAT 135:257147
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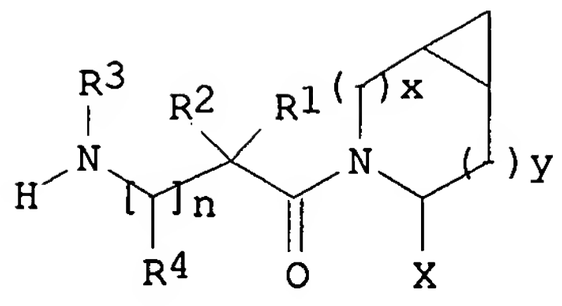

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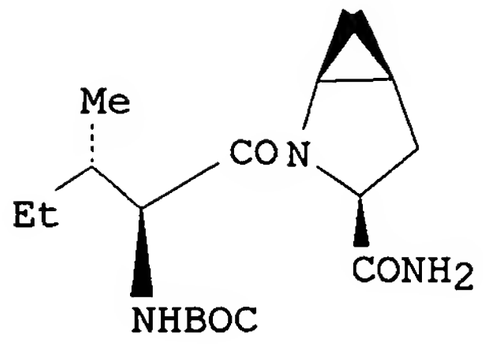
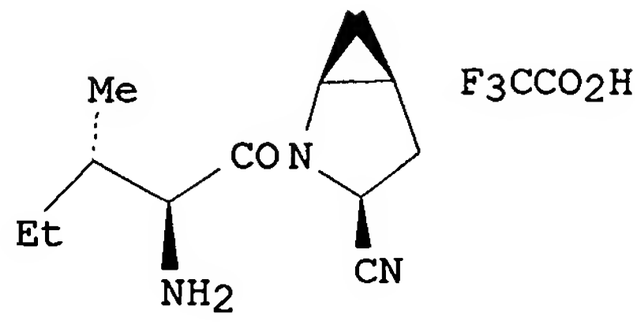


II



III

AB Dipeptidyl peptidase IV inhibiting compds. I (x = 0 or 1 and y = 0 or 1 provided that x = 1 when y = 0 and x = 0 when y = 1; n = 0, 1; X = H, CN; R1, R2, R3 and R4 = same or different and independently selected from H, (un)substituted chain or cyclic components) and the pharmaceutically acceptable salts or prodrugs (no data) were prepared Thus L-pyroglutamic acid Et ester was protected, cyclopropanated and reacted further with (S)-N-BOC-isoleucine providing an intermediate II which reacted further to yield the fused cyclopropylpyrrolidine III in 57% yield. A method is also provided for treating diabetes and related diseases, especially Type II diabetes, and other diseases by employing a title DP 4 inhibitor or a combination of DP 4 inhibitor and one or more of another antidiabetic agent such as metformin, glyburide, troglitazone, pioglitazone, rosiglitazone and/or insulin and/or one or more of a hypolipidemic agent and/or anti-obesity agent and/or other therapeutic agent.

L4 ANSWER 12 OF 45 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:639858 CAPLUS
TITLE: Design and synthesis of N-substituted glycyl 2-cyanopyrrolidines as a new class of DPP-IV inhibitors
AUTHOR(S): Brinkman, John A.; Villhauer, Edwin B.; Naderi, Goli B.; Hughes, Thomas E.; Mone, Manisha; Russell, Mary E.; Weldon, Stephen C.
CORPORATE SOURCE: Medicinal Chemistry Department, Metabolic and Cardiovascular Diseases Research, Novartis Institute of Biomedical Research, Summit, NJ, 07901, USA
SOURCE: Abstracts of Papers, 222nd ACS National Meeting, Chicago, IL, United States, August 26-30, 2001 (2001), MEDI-039. American Chemical Society: Washington, D. C.
CODEN: 69BUZP
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
AB Dipeptidyl peptidase IV (DPP-IV, EC 3.4.14.5) is a post-proline cleaving enzyme which catalyzes the cleavage of dipeptides AA-Pro (AA=amino acid residue) from the N-terminus of proteins. Inhibition of DPP-IV has been recognized as a mechanistic approach of potential value in the treatment of type 2 diabetes. Our work will describe the design and synthesis of a new class of potent, selective and stable DPP-IV inhibitors. The synthesis will focus on the use of both resin-based and solution-based chemical to incorporate

various N-substituted glycines at the P2 position of the dipeptide inhibitor. Details of the structure-activity relationships associated with variations of the P2 position will be highlighted leading to NVP-DPP728, currently in phase II clin. trials.

L4 ANSWER 13 OF 45 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:635906 CAPLUS
DOCUMENT NUMBER: 135:190422
TITLE: Inhibition of beta cell degeneration
INVENTOR(S): Carr, Richard David
PATENT ASSIGNEE(S): Novo Nordisk A/S, Den.
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001062266	A2	20010830	WO 2001-DK115	20010220 <--
WO 2001062266	A3	20020502		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
WO 2001055105	A1	20010802	WO 2001-DK45	20010122 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2001031780	A1	20011018	US 2001-767354	20010123 <--
US 6380398	B2	20020430		
EP 1259246	A2	20021127	EP 2001-DK905634	20010220
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003523396	T	20030805	JP 2001-561331	20010220
US 2002103384	A1	20020801	US 2002-76577	20020208
US 6645995	B2	20031111		

PRIORITY APPLN. INFO.:

DK 2000-295	A	20000225
DK 2000-983	A	20000623
WO 2001-DK45	W	20010122
DK 2000-112	A	20000124
US 2000-178856P	P	20000128
US 2000-216202P	P	20000706
US 2001-767354	A3	20010123
WO 2001-DK115	W	20010220

AB The present invention relates to a method preventing beta cell degeneration, such as necrosis or apoptosis of beta cells in a subject, comprising administering a DPP-IV (dipeptidyl peptidase IV) inhibitor to said subject. The invention furthermore relates to a method for increasing the number and/or the size of beta cells. The invention also relates to a method for delaying the progression of Impaired Glucose Tolerance (IGT) to type 2 diabetes

, as well as a method for delaying the progression of non-insulin demanding type 2 diabetes to insulin-demanding type 2 diabetes.

L4 ANSWER 14 OF 45 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:635436 CAPLUS
DOCUMENT NUMBER: 136:319179
TITLE: DPPIV-inhibition as treatment of type II diabetes
AUTHOR(S): Hoffmann, Torsten; Glund, Konrad; McIntosh, Christopher H. S.; Pederson, Raymond A.; Hanefeld, Markolf; Rosenkranz, Bernd; Demuth, Hans-Ulrich
CORPORATE SOURCE: Probiodrug Research GmbH, Halle, D-06120, Germany
SOURCE: International Congress Series (2001), 1218(Cell-Surface Aminopeptidases: Basic and Clinical Aspects), 381-387
CODEN: EXMDA4; ISSN: 0531-5131
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The insulin-releasing action of glucose absorbed after a meal is amplified by the concurrent release of the gut hormones (incretins), glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide 1 (GLP-1). Their rapid deactivation by DPPIV can be modulated by inhibition of the enzyme. After preclin. investigations, the drug candidate Di-[3N-((2S,3S)-2-amino-3-methyl-pentanoyl)1,3-thiazolidine] fumarate (P32/98) has entered clin. phases I and II. Phase I - A randomized and double-blind study was designed to investigate safety and tolerability of P32/98. Thirty-six healthy male volunteers received ascending single oral doses of P32/98 (7.5 to 240 mg) or a placebo. Drug administration (t = 0) was followed by a standard oral glucose tolerance test (OGTT) at t = 10 min. Safety laboratory, vital signs, 12-lead ECG, telemetry and adverse events as well as pharmacokinetic and pharmacodynamic parameters were recorded. Phase II - In a subsequent open trial, the response to a single oral dose (60 mg) of P32/98 in 24 patients was investigated. After overnight fasting and a 12-h wash-out of previous medication each patient received an OGTT at the beginning of the experiment, Seven days later the same experiment was done with drug application 15 min prior to an OGTT. Blood samples were taken for determination of P32/98, DPPIV, glucose, insulin, proinsulin, C-peptide, GLP-1. The drug was well tolerated. Parallel to the dose-dependent decrease of plasma DPPIV-activity an increase of bioactive GLP-1 was observed Accordingly, an improvement of glucose tolerance was shown in healthy volunteers as well as in diabetics. Hence. our concept - glucose tolerance improvement via incretin modulation by oral DPPIV-inhibitor therapy - has been proven successfully in patients.
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 15 OF 45 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:620287 CAPLUS
DOCUMENT NUMBER: 135:313699
TITLE: Development of glucagon-like peptide-1-based pharmaceuticals as therapeutic agents for the treatment of diabetes
AUTHOR(S): Drucker, Daniel J.
CORPORATE SOURCE: Department of Medicine, Banting and Best Diabetes Centre, Toronto General Hospital, University of Toronto, Toronto, ON, Can.
SOURCE: Current Pharmaceutical Design (2001), 7(14), 1399-1412
CODEN: CPDEFP; ISSN: 1381-6128
PUBLISHER: Bentham Science Publishers

DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with refs. Glucagon-like peptide-1 (GLP-1) is released from gut endocrine cells following nutrient ingestion and acts to regulate nutrient assimilation via effects on gastrointestinal motility, islet hormone secretion, and islet cell proliferation. Exogenous administration of GLP-1 lowers blood glucose in normal rodents and in multiple exptl. models of diabetes mellitus. Similarly, GLP-1 lowers blood glucose in normal subjects and in patients with type 2 diabetes. The therapeutic utility of the native GLP-1 mol. is limited by its rapid enzymic degradation by the serine protease dipeptidyl peptidase IV. This review highlights recent advances in the authors' understanding of GLP-1 physiol. and GLP-1 receptor signaling, and summarizes current pharmaceutical strategies directed at sustained activation of GLP-1 receptor-dependent actions for glucoregulation in vivo. Given the nutrient-dependent control of GLP-1 release, neutraceuticals or modified diets that enhance GLP-1 release from the enteroendocrine cell may exhibit glucose-lowering properties in human subjects. The utility of GLP-1 derivs. engineered for sustained action and/or DP IV-resistance, and the biol. activity of naturally occurring GLP-1-related mols. such as exendin-4 is reviewed. Circumventing DP IV-mediated incretin degradation via inhibitors that target the DP IV enzyme represents a complementary strategy for enhancing GLP-1-mediated actions in vivo. Finally, the current status of alternative GLP-1-delivery systems via the buccal and enteral mucosa is briefly summarized. The findings that the potent glucose-lowering properties of GLP-1 are preserved in diabetic subjects, taken together with the potential for GLP-1 therapy to preserve or augment β cell mass, provides a powerful impetus for development of GLP-1-based human pharmaceuticals.

REFERENCE COUNT: 171 THERE ARE 171 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

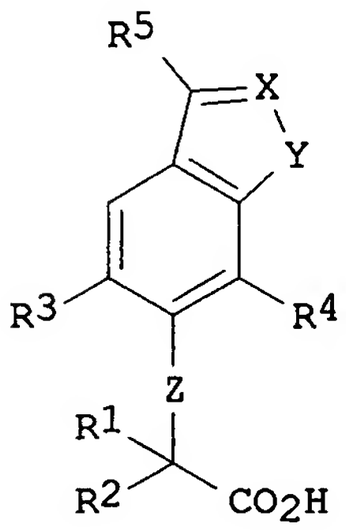
L4 ANSWER 16 OF 45 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:617987 CAPLUS
DOCUMENT NUMBER: 135:180757
TITLE: Preparation of 1,2-benzoxazolyloxyacetic acids and analogs as PPAR agonists for treatment of diabetes and lipid disorders
INVENTOR(S): Liu, Kun; Xu, Libo; Jones, A. Brian
PATENT ASSIGNEE(S): Merck & Co. Inc., USA
SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001060807	A1	20010823	WO 2001-US4636	20010214 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2400021	A1	20010823	CA 2001-2400021	20010214 <--
AU 2001038214	A5	20010827	AU 2001-38214	20010214 <--

AU 784722		B2	20060601		
EP 1259494		A1	20021127	EP 2001-910624	20010214
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
JP 2003523336		T	20030805	JP 2001-560192	20010214
PRIORITY APPLN. INFO.:				US 2000-183593P	P 20000218
				WO 2001-US4636	W 20010214

OTHER SOURCE(S): MARPAT 135:180757

GI



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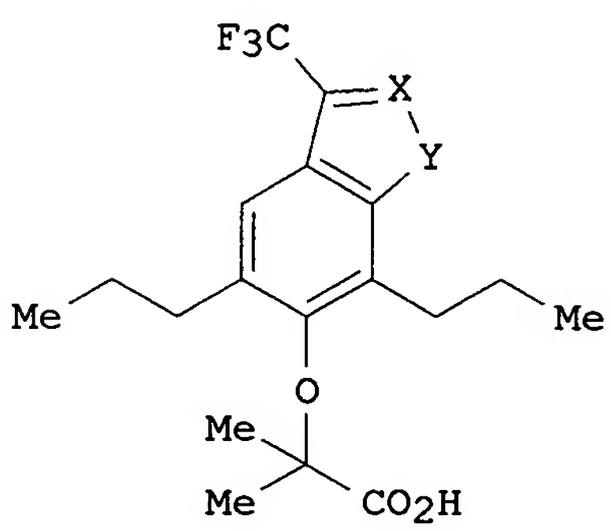


II

AB The title compds. (I) [wherein R1 and R2 = independently H, F, (halo)alkyl, (halo)alkenyl, (halo)alkynyl; or R1 and R2 may form a cycloalkyl group; R3 and R4 = independently (fluoro)alkyl, (fluoro)alkenyl, (fluoro)alkynyl, or Cl; X = N or CR; Y = O, S, nor NR; Z = O or S; R = independently H or optionally fluoro- or alkoxy-substituted (cyclo)alkyl(oxy), alkenyl(oxy), or alkynyl(oxy); R5 = H or (un)substituted alkyl, alkenyl, alkynyl, (hetero)aryl(oxy), heterocyclyl(oxy), etc.; and pharmaceutically acceptable salts and prodrugs thereof] were prepared For example, 2,4-dihydroxy-3,5-dipropyl-1',1',1'-trifluoroacetophenone oxime was acetylated and then treated with pyridine and TEA to give 5,7-dipropyl-6-hydroxy-3-trifluoromethyl-1,2-benzisoxazole. Etherification with Me α-bromoisobutyrate in the presence of Cs2CO3 in DMF, followed by saponification, afforded the 1,2-benzoxazolyloxyacetic acid (II). I are potent agonists of peroxisome proliferator activated receptor (PPAR) α and/or γ and are useful in the treatment, control, or prevention of non-insulin dependent diabetes mellitus (NIDDM), hyperglycemia, dyslipidemia, hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, atherosclerosis, obesity, vascular restenosis, inflammation, and other PPARα and/or γ mediated diseases, disorders, and conditions (no data).

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 17 OF 45 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	2001:576390 CAPLUS
DOCUMENT NUMBER:	135:236566
TITLE:	The entero-insular axis in type 2 diabetes - incretins as therapeutic agents
AUTHOR(S):	Creutzfeldt, W.
CORPORATE SOURCE:	Department of Medicine, Georg-August-University, Goettingen, Germany
SOURCE:	Experimental and Clinical Endocrinology & Diabetes (2001), 109(Suppl. 2), S288-S303 CODEN: ECEDFQ; ISSN: 0947-7349
PUBLISHER:	Johann Ambrosius Barth
DOCUMENT TYPE:	Journal; General Review

LANGUAGE: English

AB A review with 122 refs. The search for intestinal factors regulating the endocrine secretion of the pancreas started soon after the discovery of secretin, i.e. nearly 100 yr ago. Insulinotropic factors of the gut released by nutrients and stimulating insulin secretion in physiol. concns. in the presence of elevated blood glucose levels have been named incretins. Of the known gut hormones only gastric inhibitory polypeptide (GIP) and glucagon-like polypeptide-1 (GLP-1 amide) fulfill this definition. The incretin effect (i.e. the ratio between the integrated insulin response to an oral glucose load and an isoglycemic i.v. glucose infusion) is markedly diminished in patients with type 2 diabetes mellitus, while the plasma levels of GIP and GLP-1 and their responses to nutrients are in the normal range. Therefore, a reduced responsiveness of the islet B-cells to incretins has been postulated. This insensitivity of the diabetic B-cells towards incretins can be overcome by supraphysiol. (pharmacol.) concns. of GLP-1, however not of GIP. Accordingly, fasting and postprandial glucose levels can be normalized in patients with type 2 diabetes by infusions of GLP-1 [7-36]. Further studies revealed that this is partially due to the fact that GLP-1, in addition to its insulinotropic effect, also inhibits glucagon secretion and delays gastric emptying. These three antidiabetic effects qualify GLP-1 as an interesting therapeutic tool, mainly for type 2 diabetes. However, because of its short plasma half life time natural GLP-1 is not suitable for s.c. application. At present methods are being developed to improve the pharmacokinetics of GLP-1 by inhibition of the cleaving enzyme dipeptidyl peptidase IV (DPP-IV) or by synthesis of DPP-IV resistant GLP-1 analogs. Also naturally occurring GLP-1 analogs (for instance exendin-4) with a much longer half life time than GLP-1 are being tested. Thus, after 100 yr of speculations and experimentations, incretins and their analogs are emerging as new antidiabetic drugs.

REFERENCE COUNT: 125 THERE ARE 125 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 18 OF 45 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:565001 CAPLUS

DOCUMENT NUMBER: 135:137398

TITLE: Preparation of N-aminoalkanoylpyrroli(di)ne-2-carbonitriles as dipeptidyl peptidase IV inhibitors

INVENTOR(S): Kanstrup, Anders; Lundbeck, Jane Marie; Christiansen, Lise Brown

PATENT ASSIGNEE(S): Novo Nordisk A/S, Den.

SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001055105	A1	20010802	WO 2001-DK45	20010122 <--

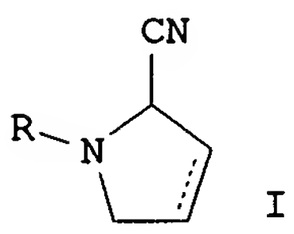
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1254113 A1 20021106 EP 2001-946849 20010122
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
JP 2003520849 T 20030708 JP 2001-555047 20010122
US 2001031780 A1 20011018 US 2001-767354 20010123 <--
US 6380398 B2 20020430
WO 2001062266 A2 20010830 WO 2001-DK115 20010220 <--
WO 2001062266 A3 20020502
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
JP 2003523396 T 20030805 JP 2001-561331 20010220
US 2001025023 A1 20010927 US 2001-790002 20010221 <--
US 7064145 B2 20060620
US 2002103384 A1 20020801 US 2002-76577 20020208
US 6645995 B2 20031111
PRIORITY APPLN. INFO.:

DK 2000-112	A	20000124
DK 2000-983	A	20000623
US 2000-178856P	P	20000128
DK 2000-295	A	20000225
US 2000-189613P	P	20000316
US 2000-216202P	P	20000706
WO 2001-DK45	W	20010122
US 2001-767354	A3	20010123
WO 2001-DK115	W	20010220

OTHER SOURCE(S): MARPAT 135:137398
GI



I

AB Title compds. [I; R = COCHR3NHR2 or COCHR7CHR3NHR2; R2 = H, (cyclo)alk(en)yl, aryl, etc.; R3,R7 = H, (cyclo)alk(en)yl, (hetero)aryl, etc.; ≥1 of R2,R3,R7 ≠ H; dashed line = optional addnl. bond] were prepared as dipeptidyl peptidase IV inhibitors (no data). Thus, (S)-2,5-dihydro-1H-pyrrole-2-carboxamide was N-acylated by (S)-Me3CCH(NHBoc)CO2H to give, after dehydration and deprotection, (S,S)-I [R = COCH(CMe3)NH2, dashed line = bond].
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 19 OF 45 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:489226 CAPLUS
DOCUMENT NUMBER: 135:56079
TITLE: Use of a hypoglycemic agent for treating impaired glucose metabolism
INVENTOR(S): Guitard, Christiane; Muller, Beate; Emmons, Rebecca
PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis-Erfindungen Verwaltungsgesellschaft m.b.H.
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001047514	A1	20010705	WO 2000-EP12174	20001204 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2393083	A1	20010705	CA 2000-2393083	20001204 <--
EP 1239854	A1	20020918	EP 2000-990641	20001204
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2000016631	A	20030107	BR 2000-16631	20001204
CN 1413107	A	20030423	CN 2000-817649	20001204
JP 2003518496	T	20030610	JP 2001-548109	20001204
NZ 519231	A	20040528	NZ 2000-519231	20001204
AU 777776	B2	20041028	AU 2001-30059	20001204
RU 2264811	C2	20051127	RU 2002-119558	20001204
NZ 531929	A	20060127	NZ 2000-531929	20001204
HU 200600522	A2	20061128	HU 2006-522	20001204
CN 1911221	A	20070214	CN 2006-10115998	20001204
US 2001016586	A1	20010823	US 2000-731139	20001206 <--
US 6949555	B2	20050927		
NO 2002002979	A	20020620	NO 2002-2979	20020620
ZA 2002004959	A	20030203	ZA 2002-4959	20020620
US 2004242647	A1	20041202	US 2004-885057	20040706
US 2005043362	A1	20050224	US 2004-939002	20040910
AU 2005200398	A1	20050224	AU 2005-200398	20050121
US 2006122244	A1	20060608	US 2006-339188	20060125
JP 2006328091	A	20061207	JP 2006-249499	20060914
US 2007032538	A1	20070208	US 2006-581891	20061017

PRIORITY APPLN. INFO.:	EP 1999-125761	A 19991223
	CN 2000-817649	A3 20001204
	JP 2001-548109	A3 20001204
	WO 2000-EP12174	W 20001204
	US 2000-731139	A3 20001206
	US 2004-885057	B1 20040706
	US 2006-339188	A1 20060125

AB The invention discloses the use of a hypoglycemic agent, or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for the prevention or delay of the progression to overt diabetes , especially type 2, prevention or reduction of microvascular complications (e.g. retinopathy, neuropathy, nephropathy), prevention or reduction of excessive cardiovascular morbidity (eg. myocardial infarction, arterial occlusive disease, atherosclerosis and stroke) and cardiovascular mortality, prevention of cancer and reduction of cancer deaths. Addnl., the invention relates to the use of a treatment for diseases and conditions that are associated with impaired glucose metabolism, impaired glucose tolerance, or impaired fasting glucose. Formulations of nateglinide are included.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 20 OF 45 CAPLUS

ACCESSION NUMBER: 2001:202250 CAPLUS
TITLE: N-substitututed glycyl 2-cyanopyrrolidines as a new family of DPP-IV inhibitors and their potential use in type 2 diabetes
AUTHOR(S): Villhauer, Edwin B.; Anderson, Robert C.; Balkan, Bork; Barilla, Denise; Brinkman, John A.; Dunn, Elina; Dunning, Beth; Graham, Elizabeth D.; Gu, Huiping H.; Gutierrez, Carmen M.; Hamilton, Brenda H.; Kwasnik, Lori A.; Li, Xue; Mangold, Bonnie L.; Maniara, Wieslawa M.; Miserendino-Molteni, Rocca; Mone, Manisha; Naderi, Goli B.; Ramos, Kathy L.; Russell, Mary E.; Rothenberg, Paul L.; Tullman, Robert H.; Valentin, Michele; Walter, R. Erik; Weldon, Stephen C.; Hughes, Thomas E.
CORPORATE SOURCE: Medicinal Chemistry Department, Metabolic and Cardiovascular Diseases Research, Novartis Institute of Biomedical Research, Summit, NJ, 07901-1398, USA
SOURCE: Abstracts of Papers, 221st ACS National Meeting, San Diego, CA, United States, April 1-5, 2001 (2001) MEDI-343
CODEN: 69FZD4
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal; Meeting Abstract
LANGUAGE: English
AB Inhibition of dipeptidyl peptidase IV (DPP-IV, EC 3.4.14.5) has been recognized as a mechanistic approach of potential value in the treatment of type 2 diabetes. We will describe the design and synthesis of a new class of potent, selective and stable DPP-IV inhibitors. The coupling of a resin-based generation of diverse N-substituted glycines with a solution-based amide to nitrile conversion will be discussed. An extensive SAR profile will be detailed. The potential use of these inhibitors for type 2 diabetes will be highlighted by describing the pharmacol. profile of our development candidate; NVP-DPP728, currently in phase II clin. trials.

=> FIL STNGUIDE

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	70.54	70.75

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-15.60	-15.60

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LAST RELOADED: May 4, 2007 (20070504/UP).

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CAN --------- List of CA abstract numbers without answer numbers
CBIB -------- AN, plus Compressed Bibliographic Data
CLASS ------- IPC, NCL, ECLA, FTERM
DALL -------- ALL, delimited (end of each field identified)
DMAX -------- MAX, delimited for post-processing
FAM --------- AN, PI and PRAI in table, plus Patent Family data
FBIB -------- AN, BIB, plus Patent FAM
IND --------- Indexing data
IPC --------- International Patent Classifications
MAX --------- ALL, plus Patent FAM, RE
PATS -------- PI, SO
SAM --------- CC, SX, TI, ST, IT
SCAN -------- CC, SX, TI, ST, IT (random display, no answer numbers;
              SCAN must be entered on the same line as the DISPLAY,
              e.g., D SCAN or DISPLAY SCAN)
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IABS -------- ABS, indented with text labels
IALL -------- ALL, indented with text labels
IBIB -------- BIB, indented with text labels
IMAX -------- MAX, indented with text labels
ISTD -------- STD, indented with text labels

OBIB -------- AN, plus Bibliographic Data (original)
OIBIB ------- OBIB, indented with text labels

SBIB -------- BIB, no citations
SIBIB ------- IBIB, no citations

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              containing hit terms
HITRN ------- HIT RN and its text modification
HITSTR ------ HIT RN, its text modification, its CA index name, and
              its structure diagram
HITSEQ ------ HIT RN, its text modification, its CA index name, its
              structure diagram, plus NTE and SEQ fields
FHITSTR ----- First HIT RN, its text modification, its CA index name, and
              its structure diagram
FHITSEQ ----- First HIT RN, its text modification, its CA index name, its
              structure diagram, plus NTE and SEQ fields
KWIC -------- Hit term plus 20 words on either side
OCC --------- Number of occurrence of hit term and field in which it occurs

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TI,IND; TI,SO.  You may specify the format fields in any order and the
information will be displayed in the same order as the format
specification.

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FHITSTR, HITSEQ, FHITSEQ, KWIC, and OCC) may be used with DISPLAY ACC
to view a specified Accession Number.
ENTER DISPLAY FORMAT (BIB):abs

L4   ANSWER 21 OF 45  CAPLUS  COPYRIGHT 2007 ACS on STN
AB   Incretin hormones importantly enhance postprandial insulin secretion but
     are rapidly degraded to inactive metabolites by ubiquitous
     dipeptidyl peptidase IV.  The concns. of the
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intact biol. active hormones remain largely unknown. Using newly developed assays for intact glucagon-like peptide (GLP)-1 and glucose-dependent insulinotropic polypeptide (GIP), we measured plasma concns. after a mixed breakfast meal (566 kcal) in 12 type 2 diabetic patients (age 57 yr [range 49-67], BMI 31 kg/m2 [27-38], and HbA1c 9.2% [7.0-12.5]) and 12 matched healthy subjects. The patients had fasting hyperglycemia (10.7 mmol/l [8.0-14.8]) increasing to 14.6 mmol/l (11.5-21.5) 75 min after meal ingestion. Fasting levels of insulin and C-peptide were similar to those of the healthy subjects, but the postprandial responses were reduced and delayed. Fasting levels and meal responses were similar between patients and healthy subjects for total GIP (intact + metabolite) as well as intact GIP, except for a small decrease in the patients at 120 min; integrated areas for intact hormone (area under the curve [AUC]INT) averaged 52±4% (for patients) vs. 56±3% (for control subjects) of total hormone AUC (AUCTOT). AUCINT for GLP-1 averaged 48±2% (for patients) vs. 51±5% (for control subjects) of AUCTOT. AUCTOT for GLP-1 as well as AUCINT tended to be reduced in the patients (P = 0.2 and 0.07, resp.); but the profile of the intact GLP-1 response was characterized by a small early rise (30-45 min) and a significantly reduced late phase (75-150 min) (P < 0.02). The measurement of intact incretin hormones revealed that total as well as intact GIP responses were minimally decreased in patients with type 2 diabetes, whereas the late intact GLP-1 response was strongly reduced, supporting the hypothesis that an impaired function of GLP-1 as a transmitter in the enteroinsular axis contributes to the inappropriate insulin secretion in type 2 diabetes.

L4 ANSWER 22 OF 45 CAPLUS COPYRIGHT 2007 ACS on STN

AB The incretin GIP (glucose-dependent insulinotropic polypeptide), a 42 amino acid peptide, is released from the K-cells of the small intestine into the blood in response to oral nutrient ingestion. GIP inhibits the secretion of gastric acid and promotes the release of insulin from pancreatic islet cells. A study was conducted in which N- and C-terminal truncated fragments as well as various GIP analogs with a reduced peptide bond or alterations of the amino acids close to the dipeptidyl peptidase IV (DPIV) specific cleavage site were synthesized with the goal of improving DPIV-resistance and a prolonged half-time. Findings indicated that DPIV-resistant analogs of GIP1-30 could be synthesized. The introduction of D-amino acids in the P1 and P1'-position resulted in a slight reduction in binding and bioactivity. The examined C-terminal truncated fragments showed no binding affinity, whereas the antagonistic N-terminal truncated fragments were able to bind to transfected rat GIP receptor. These results emphasize the hypothesis of an existing one-receptor-two-interaction-sites-model which was shown for peptides of the GRF-family. Concerning the potential use of GIP analogs in the treatment of type II diabetes mellitus, these results offer the possibility of synthesizing analogs with reasonable half-life times and physiol. relevant binding affinities and bioactivity.

L4 ANSWER 23 OF 45 CAPLUS COPYRIGHT 2007 ACS on STN

AB This is the second patent application from Novartis describing N-substituted-2-cyanopyrrolidines as inhibitors of dipeptidyl peptidase IV (DPP-IV). DPP-IV is a serine protease which cleaves Xaa-Pro- or Xaa-Ala-amino terminal sequences from biol. active peptides, transforming them into inactive or even antagonistic species. Among them is glucagon-like peptide 1 (GLP-1), a major stimulator of pancreatic insulin secretion with addnl. properties in lowering the blood glucose level, which is normally secreted in response to food ingestion. By inhibiting DPP-IV the endogenous GLP-1 is preserved for longer periods, the inhibitors being useful in the treatment of the non-insulin-dependent diabetes mellitus (NIDDM), obesity, arthritis, osteoporosis and other diseases generated or enhanced by impaired glucose tolerance. The compds. claimed in this application are

novel N-substituted 2-cyanopyrrolidines bearing adamantyl moieties as biocompatible lipophylic groups; their low nanomolar level of DPP-IV inhibition, as well as their in vivo therapeutic profile, are improved as compared with the results obtained in previous studies.

L4 ANSWER 24 OF 45 CAPLUS COPYRIGHT 2007 ACS on STN

AB Glucagon-like peptide-1(7-36)amide (tGLP-1) has attracted considerable potential as a possible therapeutic agent for type 2 diabetes. However, tGLP-1 is rapidly inactivated in vivo by the exopeptidase dipeptidyl peptidase IV (DPP IV), thereby terminating its insulin releasing activity. The present study has examined the ability of a novel analog, His7-glucitol tGLP-1 to resist plasma degradation and enhance the insulin-releasing and antihyperglycemic activity of the peptide in 20-25-wk-old obese diabetic ob/ob mice. Degradation of native tGLP-1 by incubation at 37° with obese mouse plasma was clearly evident after 3 h (35% intact). After 6 h, more than 87% of tGLP-1 was converted to GLP-1(9-36)amide and two further N-terminal fragments, GLP-1(7-28) and GLP-1(9-28). In contrast, His7-glucitol tGLP-1 was completely resistant to N-terminal degradation The formation of GLP-1(9-36)amide from native tGLP-1 was almost totally abolished by addition of diprotin A, a specific inhibitor of DPP IV. Effects of tGLP-1 and His7-glucitol tGLP-1 were examined in overnight fasted obese mice following i.p. injection of either peptide (30 nmol/kg) together with glucose (18 mmol/kg) or in association with feeding. Plasma glucose was significantly lower and insulin response greater following administration of His7-glucitol tGLP-1 as compared to glucose alone. Native tGLP-1 lacked antidiabetic effects under the conditions employed, and neither peptide influenced the glucose-lowering action of exogenous insulin (50 units/kg). Twice daily s.c. injection of ob/ob mice with His7-glucitol tGLP-1 (10 nmol/kg) for 7 days reduced fasting hyperglycemia and greatly augmented the plasma insulin response to the peptides given in association with feeding. These data demonstrate that His7-glucitol tGLP-1 displays resistance to plasma DPP IV degradation and exhibits antihyperglycemic activity and substantially enhanced insulin-releasing action in a commonly used animal model of type 2 diabetes.

L4 ANSWER 25 OF 45 CAPLUS COPYRIGHT 2007 ACS on STN

AB Gastric inhibitory polypeptide (GIP) is susceptible to degradation, but only recently has dipeptidyl peptidase IV been identified as the enzyme responsible. Most RIAs recognize both intact GIP-(1-42) and the noninsulinotropic N-terminally truncated metabolite, GIP-(3-42), hampering measurement of plasma concns. The mol. nature of GIP was examined using HPLC and a newly developed RIA specific for the intact N-terminus of human GIP. In healthy subjects after a mixed meal, intact GIP (N-terminal RIA) accounted for 37.0±2.5% of the total immunoreactivity determined by C-terminal assay. High pressure liquid chromatog. anal. of fasting samples by C-terminal assay revealed one major peak (73.8±2.9%) coeluting with GIP-(3-42). One hour postprandially, two major peaks were detected, corresponding to GIP-(3-42) and GIP-(1-42) (58.1±2.7% and 35.7±4.2%, resp.). GIP-(3-42) was not detected by N-terminal assay; the major peak coeluted with intact GIP (86.4±5.8% and 81.3±0.9%, 0 and 1 h, resp.). After iv infusion, intact GIP constituted 37.1±4.1% and 41.3±3.4% of the total immunoreactivity in healthy and type 2 diabetic subjects, resp. The plasma t1/2 was shorter ($P < 0.0001$) when determined by N-terminal compared with C-terminal assay (7.3±1.0 vs. 16.8±1.6 and 5.2±0.6 vs. 12.9±0.9 min, healthy and diabetic subjects, resp.), and both t1/2 were shorter in the diabetic group ($P < 0.05$). The authors conclude that dipeptidyl peptidase IV is important in GIP metabolism in humans in vivo, and that an N-terminally directed assay is required for determination of plasma concns. of biol. active GIP.

L4 ANSWER 26 OF 45 CAPLUS COPYRIGHT 2007 ACS on STN

AB Dipeptidyl peptidase IV (DPP IV, also known as CD26; EC 3.4, 14.5) is a non-integrin receptor glycoprotein with multiple functions, including cell adhesion, cellular trafficking through the extracellular matrix and co-stimulatory potential during T cell activation. By virtue of its exopeptidase activity, DPP IV plays a key regulatory role in the metabolism of peptide hormones. Based on data emerging from different biomedical specialties, it appears worthwhile to highlight the different facets of DPP IV in nutrition, immune responses and peptide hormone metabolism The presentation of the complex regulatory circuits in which DPP IV appears to be involved may also serve as a note of caution, in view of attempts to apply selective inhibitors of DPP IV enzymic activity for the treatment of disease, e.g. Type II diabetes.

L4 ANSWER 27 OF 45 CAPLUS COPYRIGHT 2007 ACS on STN

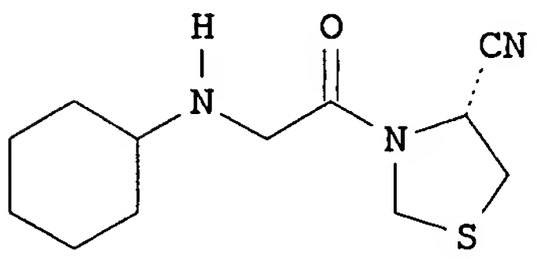
AB The use of metformin in the preparation of pharmaceutical compns. useful for inhibiting the enzyme dipeptidyl peptidase IV , in particular for increasing the plasma concentration of Glucagon-Like Peptide-1 (GPL-1), is described. Metformin was administered at 850 mg orally t.i.d. for 14 days to obese non-diabetic male patients, aged 30-60 yr. Metformin increased the plasma levels of the active forms of GPL-1 after an oral glucose load, without modifying the basal hormone concentration Tablets of 850 mg metformin are administered 3 times a day before breakfast, lunch and dinner.

L4 ANSWER 28 OF 45 CAPLUS COPYRIGHT 2007 ACS on STN

AB We explored whether inhibition of the enzyme dipeptidyl peptidase IV (DPP IV) increases endogenous levels of glucagon-like peptide-1 (GLP-1) and improves glucose tolerance and insulin secretion in mice. Glucose (150 mg) was administered through a gastric gavage with or without the inhibitor of dipeptidyl peptidase IV, valine-pyrrolidide (100 μmol/kg), in high-fat fed glucose intolerant or control C57BL/6J mice. The increase in plasma GLP-1 after gastric glucose was potentiated by dipeptidyl peptidase IV inhibition ($P<0.05$). Valine-pyrrolidide also potentiated the plasma insulin response to gastric glucose and improved the glucose tolerance in both groups of mice ($P<0.001$). In contrast, valine-pyrrolidide did not affect glucose-stimulated insulin secretion from isolated islets. This suggests that valine-pyrrolidide improves insulin secretion and glucose tolerance through indirect action, probably through augmentation of levels of GLP-1 and other incretin hormones. Therefore, inhibition of dipeptidyl peptidase IV activity is feasible to exploit as a treatment for glucose intolerance and type 2 diabetes.

L4 ANSWER 29 OF 45 CAPLUS COPYRIGHT 2007 ACS on STN

GI



II

AB RNHCH2COR5 [I; R = (cyclo)alkyl, CH2CH2NHR1, CH2CH2R2, CH2CH2CH(R3)2, (CH2)3R4; R1 = (un)substituted pyridinyl or -pyrimidinyl; R2,R3 = (un)substituted Ph; R4 = 2-oxopyrrolidinyl or alkoxy; R5 = (R)-4-cyano-3-thiazolidinyl] were prepared Thus, (R)-thiazolidine-4-

carboxamide was N-acylated by Me3CO2CNRCH2CO2H (R = cyclohexyl)(preparation each given) and the product dehydrated to give, after deprotection, title compound II. Data for biol. activity of I were given.

L4 ANSWER 30 OF 45 CAPLUS COPYRIGHT 2007 ACS on STN
AB A review with 50 refs. Type 2 diabetes is a chronic metabolic derangement that results from defects in both insulin action and secretion. New thiazolidinedione insulin sensitizers have been recently launched. New approaches with mechanisms different from current therapies are being explored, including novel ligands of peroxisome proliferator-activated receptor, glucagon receptor antagonists, dipeptidyl peptidase IV inhibitors, and insulin receptor activators.

=> d ibib abs hitstr 21-30
YOU HAVE REQUESTED DATA FROM FILE 'CAPLUS' - CONTINUE? (Y)/N:y

L4 ANSWER 21 OF 45 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:175315 CAPLUS
DOCUMENT NUMBER: 134:339067
TITLE: Reduced postprandial concentrations of intact biologically active glucagon-like peptide 1 in type 2 diabetic patients
AUTHOR(S): Vilsboll, Tina; Krarup, Thure; Deacon, Carolyn F.; Madsbad, Sten; Holst, Jens J.
CORPORATE SOURCE: Department of Internal Medicine F, Gentofte Hospital, Copenhagen, Den.
SOURCE: Diabetes (2001), 50(3), 609-613
CODEN: DIAEAZ; ISSN: 0012-1797
PUBLISHER: American Diabetes Association
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Incretin hormones importantly enhance postprandial insulin secretion but are rapidly degraded to inactive metabolites by ubiquitous dipeptidyl peptidase IV. The concns. of the intact biol. active hormones remain largely unknown. Using newly developed assays for intact glucagon-like peptide (GLP)-1 and glucose-dependent insulinotropic polypeptide (GIP), we measured plasma concns. after a mixed breakfast meal (566 kcal) in 12 type 2 diabetic patients (age 57 yr [range 49-67], BMI 31 kg/m2 [27-38], and HbA1c 9.2% [7.0-12.5]) and 12 matched healthy subjects. The patients had fasting hyperglycemia (10.7 mmol/l [8.0-14.8]) increasing to 14.6 mmol/l (11.5-21.5) 75 min after meal ingestion. Fasting levels of insulin and C-peptide were similar to those of the healthy subjects, but the postprandial responses were reduced and delayed. Fasting levels and meal responses were similar between patients and healthy subjects for total GIP (intact + metabolite) as well as intact GIP, except for a small decrease in the patients at 120 min; integrated areas for intact hormone (area under the curve [AUC]INT) averaged 52±4% (for patients) vs. 56±3% (for control subjects) of total hormone AUC (AUCTOT). AUCINT for GLP-1 averaged 48±2% (for patients) vs. 51±5% (for control subjects) of AUCTOT. AUCTOT for GLP-1 as well as AUCINT tended to be reduced in the patients (P = 0.2 and 0.07, resp.); but the profile of the intact GLP-1 response was characterized by a small early rise (30-45 min) and a significantly reduced late phase (75-150 min) (P < 0.02). The measurement of intact incretin hormones revealed that total as well as intact GIP responses were minimally decreased in patients with type 2 diabetes, whereas the late intact GLP-1 response was strongly reduced, supporting the hypothesis that an impaired function of GLP-1 as a transmitter in the enteroinsular axis contributes to the inappropriate

insulin secretion in type 2 diabetes.
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 22 OF 45 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:868282 CAPLUS
DOCUMENT NUMBER: 135:28620
TITLE: Analogs of glucose-dependent insulinotropic polypeptide with increased dipeptidyl peptidase IV resistance
AUTHOR(S): Kuhn-Wache, Kerstin; Manhart, Susanne; Hoffmann, Torsten; Hinke, Simon A.; Gelling, R.; Pederson, Raymond A.; McIntosh, Christopher H. S.; Demuth, Hans-Ullrich
CORPORATE SOURCE: Probiodrug GmbH, Halle/Saale, 06120, Germany
SOURCE: Advances in Experimental Medicine and Biology (2000), 477, 187-195
CODEN: AEMBAP; ISSN: 0065-2598
PUBLISHER: Kluwer Academic/Plenum Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The incretin GIP (glucose-dependent insulinotropic polypeptide), a 42 amino acid peptide, is released from the K-cells of the small intestine into the blood in response to oral nutrient ingestion. GIP inhibits the secretion of gastric acid and promotes the release of insulin from pancreatic islet cells. A study was conducted in which N- and C-terminal truncated fragments as well as various GIP analogs with a reduced peptide bond or alterations of the amino acids close to the dipeptidyl peptidase IV (DPIV) specific cleavage site were synthesized with the goal of improving DPIV-resistance and a prolonged half-time. Findings indicated that DPIV-resistant analogs of GIP1-30 could be synthesized. The introduction of D-amino acids in the P1 and P1'-position resulted in a slight reduction in binding and bioactivity. The examined C-terminal truncated fragments showed no binding affinity, whereas the antagonistic N-terminal truncated fragments were able to bind to transfected rat GIP receptor. These results emphasize the hypothesis of an existing one-receptor-two-interaction-sites-model which was shown for peptides of the GRF-family. Concerning the potential use of GIP analogs in the treatment of type II diabetes mellitus, these results offer the possibility of synthesizing analogs with reasonable half-life times and physiol. relevant binding affinities and bioactivity.
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 23 OF 45 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:857124 CAPLUS
TITLE: Novel N-substituted-2-cyanopyrrolidines as potent inhibitors of dipeptidyl peptidase IV in the treatment of non-insulin-dependent diabetes mellitus
AUTHOR(S): Anon.
SOURCE: Expert Opinion on Therapeutic Patents (2000), 10(12), 1937-1942
CODEN: EOTPEG; ISSN: 1354-3776
PUBLISHER: Ashley Publications Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB This is the second patent application from Novartis describing N-substituted-2-cyanopyrrolidines as inhibitors of dipeptidyl peptidase IV (DPP-IV). DPP-IV is a serine protease which cleaves Xaa-Pro- or Xaa-Ala-amino terminal sequences from biol. active peptides, transforming them into inactive or even antagonistic species. Among them is glucagon-like peptide 1 (GLP-1), a

major stimulator of pancreatic insulin secretion with addnl. properties in lowering the blood glucose level, which is normally secreted in response to food ingestion. By inhibiting DPP-IV the endogenous GLP-1 is preserved for longer periods, the inhibitors being useful in the treatment of the non-insulin-dependent diabetes mellitus (NIDDM), obesity, arthritis, osteoporosis and other diseases generated or enhanced by impaired glucose tolerance. The compds. claimed in this application are novel N-substituted 2-cyanopyrrolidines bearing adamantyl moieties as biocompatible lipophylic groups; their low nanomolar level of DPP-IV inhibition, as well as their in vivo therapeutic profile, are improved as compared with the results obtained in previous studies.

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 24 OF 45 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:853946 CAPLUS
DOCUMENT NUMBER: 134:142074
TITLE: Degradation and glycemic effects of His7-glucitol glucagon-like peptide-1(7-36)amide in obese diabetic ob/ob mice
AUTHOR(S): O'Harte, F. P. M.; Mooney, M. H.; Kelly, C. M. N.; McKillop, A. M.; Flatt, P. R.
CORPORATE SOURCE: School of Biomedical Sciences, University of Ulster, Coleraine, BT52 1SA, UK
SOURCE: Regulatory Peptides (2001), 96(3), 95-104
CODEN: REPPDY; ISSN: 0167-0115
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Glucagon-like peptide-1(7-36)amide (tGLP-1) has attracted considerable potential as a possible therapeutic agent for type 2 diabetes. However, tGLP-1 is rapidly inactivated in vivo by the exopeptidase dipeptidyl peptidase IV (DPP IV), thereby terminating its insulin releasing activity. The present study has examined the ability of a novel analog, His7-glucitol tGLP-1 to resist plasma degradation and enhance the insulin-releasing and antihyperglycemic activity of the peptide in 20-25-wk-old obese diabetic ob/ob mice. Degradation of native tGLP-1 by incubation at 37° with obese mouse plasma was clearly evident after 3 h (35% intact). After 6 h, more than 87% of tGLP-1 was converted to GLP-1(9-36)amide and two further N-terminal fragments, GLP-1(7-28) and GLP-1(9-28). In contrast, His7-glucitol tGLP-1 was completely resistant to N-terminal degradation The formation of GLP-1(9-36)amide from native tGLP-1 was almost totally abolished by addition of diprotin A, a specific inhibitor of DPP IV. Effects of tGLP-1 and His7-glucitol tGLP-1 were examined in overnight fasted obese mice following i.p. injection of either peptide (30 nmol/kg) together with glucose (18 mmol/kg) or in association with feeding. Plasma glucose was significantly lower and insulin response greater following administration of His7-glucitol tGLP-1 as compared to glucose alone. Native tGLP-1 lacked antidiabetic effects under the conditions employed, and neither peptide influenced the glucose-lowering action of exogenous insulin (50 units/kg). Twice daily s.c. injection of ob/ob mice with His7-glucitol tGLP-1 (10 nmol/kg) for 7 days reduced fasting hyperglycemia and greatly augmented the plasma insulin response to the peptides given in association with feeding. These data demonstrate that His7-glucitol tGLP-1 displays resistance to plasma DPP IV degradation and exhibits antihyperglycemic activity and substantially enhanced insulin-releasing action in a commonly used animal model of type 2 diabetes.

REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 25 OF 45 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:757346 CAPLUS

DOCUMENT NUMBER: 133:344749
TITLE: Degradation of endogenous and exogenous gastric inhibitory polypeptide in healthy and in type 2 diabetic subjects as revealed using a new assay for the intact peptide
AUTHOR(S): Deacon, Carolyn F.; Nauck, Michael A.; Meier, Juris; Hucking, Katrin; Holst, Jens Juul
CORPORATE SOURCE: Department of Medical Physiology, The Panum Institute, University of Copenhagen, Copenhagen, DK-2200, Den.
SOURCE: Journal of Clinical Endocrinology and Metabolism (2000), 85(10), 3575-3581
CODEN: JCEMAZ; ISSN: 0021-972X
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Gastric inhibitory polypeptide (GIP) is susceptible to degradation, but only recently has dipeptidyl peptidase IV been identified as the enzyme responsible. Most RIAs recognize both intact GIP-(1-42) and the noninsulinotropic N-terminally truncated metabolite, GIP-(3-42), hampering measurement of plasma concns. The mol. nature of GIP was examined using HPLC and a newly developed RIA specific for the intact N-terminus of human GIP. In healthy subjects after a mixed meal, intact GIP (N-terminal RIA) accounted for 37.0±2.5% of the total immunoreactivity determined by C-terminal assay. High pressure liquid chromatog. anal. of fasting samples by C-terminal assay revealed one major peak (73.8±2.9%) coeluting with GIP-(3-42). One hour postprandially, two major peaks were detected, corresponding to GIP-(3-42) and GIP-(1-42) (58.1±2.7% and 35.7±4.2%, resp.). GIP-(3-42) was not detected by N-terminal assay; the major peak coeluted with intact GIP (86.4±5.8% and 81.3±0.9%, 0 and 1 h, resp.). After iv infusion, intact GIP constituted 37.1±4.1% and 41.3±3.4% of the total immunoreactivity in healthy and type 2 diabetic subjects, resp. The plasma t1/2 was shorter ($P < 0.0001$) when determined by N-terminal compared with C-terminal assay (7.3±1.0 vs. 16.8±1.6 and 5.2±0.6 vs. 12.9±0.9 min, healthy and diabetic subjects, resp.), and both t1/2 were shorter in the diabetic group ($P < 0.05$). The authors conclude that dipeptidyl peptidase IV is important in GIP metabolism in humans in vivo, and that an N-terminally directed assay is required for determination of plasma concns. of biol. active GIP.
REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 26 OF 45 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:649587 CAPLUS
DOCUMENT NUMBER: 134:206508
TITLE: A guardian angel: the involvement of dipeptidyl peptidase IV in psychoneuroendocrine function, nutrition and immune defence
AUTHOR(S): Hildebrandt, Martin; Reutter, Werner; Arck, Petra; Rose, Matthias; Klapp, Burghard F.
CORPORATE SOURCE: Charite Campus Virchow-Klinikum, Medizinische Fakultat der Humboldt-Universitat zu Berlin, Berlin, D-13353, Germany
SOURCE: Clinical Science (2000), 99(2), 93-104
CODEN: CSCIAE; ISSN: 0143-5221
PUBLISHER: Portland Press Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Dipeptidyl peptidase IV (DPP IV, also known as CD26; EC 3.4, 14.5) is a non-integrin receptor glycoprotein with multiple functions, including cell adhesion, cellular trafficking through

the extracellular matrix and co-stimulatory potential during T cell activation. By virtue of its exopeptidase activity, DPP IV plays a key regulatory role in the metabolism of peptide hormones. Based on data emerging from different biomedical specialties, it appears worthwhile to highlight the different facets of DPP IV in nutrition, immune responses and peptide hormone metabolism The presentation of the complex regulatory circuits in which DPP IV appears to be involved may also serve as a note of caution, in view of attempts to apply selective inhibitors of DPP IV enzymic activity for the treatment of disease, e.g. Type II diabetes.

REFERENCE COUNT: 127 THERE ARE 127 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 27 OF 45 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:645841 CAPLUS
DOCUMENT NUMBER: 133:227829
TITLE: Use of metformin in the preparation of pharmaceutical compositions capable of inhibiting the enzyme dipeptidyl peptidase IV
INVENTOR(S): Mannucci, Edoardo; Rotella, Carlo Maria; Ognibene, Agostino
PATENT ASSIGNEE(S): L. Molteni & C. Dei Fratelli Alitti Societa' Di Esercizio S.p.A., Italy
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000053171	A1	20000914	WO 2000-EP1849	20000303 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
IT 1307844	B1	20011119	IT 1999-FI40	19990305 <--
IT 99FI0215	A1	20010419	IT 1999-FI215	19991019 <--
IT 1307808	B1	20011119		

PRIORITY APPLN. INFO.: IT 1999-FI40 A 19990305
IT 1999-FI215 A 19991019

AB The use of metformin in the preparation of pharmaceutical compns. useful for inhibiting the enzyme dipeptidyl peptidase IV , in particular for increasing the plasma concentration of Glucagon-Like Peptide-1 (GPL-1), is described. Metformin was administered at 850 mg orally t.i.d. for 14 days to obese non-diabetic male patients, aged 30-60 yr. Metformin increased the plasma levels of the active forms of GPL-1 after an oral glucose load, without modifying the basal hormone concentration Tablets of 850 mg metformin are administered 3 times a day before breakfast, lunch and dinner.

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 28 OF 45 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:622123 CAPLUS
DOCUMENT NUMBER: 133:359069
TITLE: Improved glucose tolerance and insulin secretion by

inhibition of dipeptidyl peptidase IV in mice

AUTHOR(S): Ahren, B.; Holst, J. J.; Martensson, H.; Balkan, B.

CORPORATE SOURCE: Malmo University Hospital, Department of Medicine, Lund University, Malmo, S-205 02, Swed.

SOURCE: European Journal of Pharmacology (2000), 404(1/2), 239-245
CODEN: EJPHAZ; ISSN: 0014-2999

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We explored whether inhibition of the enzyme dipeptidyl peptidase IV (DPP IV) increases endogenous levels of glucagon-like peptide-1 (GLP-1) and improves glucose tolerance and insulin secretion in mice. Glucose (150 mg) was administered through a gastric gavage with or without the inhibitor of dipeptidyl peptidase IV, valine-pyrrolidide (100 μmol/kg), in high-fat fed glucose intolerant or control C57BL/6J mice. The increase in plasma GLP-1 after gastric glucose was potentiated by dipeptidyl peptidase IV inhibition ($P<0.05$). Valine-pyrrolidide also potentiated the plasma insulin response to gastric glucose and improved the glucose tolerance in both groups of mice ($P<0.001$). In contrast, valine-pyrrolidide did not affect glucose-stimulated insulin secretion from isolated islets. This suggests that valine-pyrrolidide improves insulin secretion and glucose tolerance through indirect action, probably through augmentation of levels of GLP-1 and other incretin hormones. Therefore, inhibition of dipeptidyl peptidase IV activity is feasible to exploit as a treatment for glucose intolerance and type 2 diabetes.

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 29 OF 45 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:606862 CAPLUS

DOCUMENT NUMBER: 133:193135

TITLE: Preparation of 3-[(alkylamino)acetyl]-4-cyanothiazolidines as dipeptidyl peptidase IV inhibitors

INVENTOR(S): Villhauer, Edwin Bernard

PATENT ASSIGNEE(S): Novartis A.-G., Switz.

SOURCE: U.S., 11 pp.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

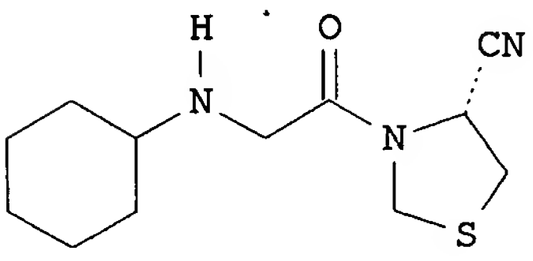
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6110949	A	20000829	US 1999-339503	19990624 <--

PRIORITY APPLN. INFO.: US 1999-339503 19990624

OTHER SOURCE(S): MARPAT 133:193135

GI



II

AB RNHCH2COR5 [I; R = (cyclo)alkyl, CH2CH2NHR1, CH2CH2R2, CH2CH2CH(R3)2, (CH2)3R4; R1 = (un)substituted pyridinyl or -pyrimidinyl; R2,R3 = (un)substituted Ph; R4 = 2-oxopyrrolidinyl or alkoxy; R5 = (R)-4-cyano-3-thiazolidinyl] were prepared Thus, (R)-thiazolidine-4-carboxamide was N-acylated by Me3CO2CNRCH2CO2H (R = cyclohexyl)(preparation each given) and the product dehydrated to give, after deprotection, title compound II. Data for biol. activity of I were given.

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 30 OF 45 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:584139 CAPLUS

DOCUMENT NUMBER: 133:246700

TITLE: New approaches in the treatment of type 2 diabetes

AUTHOR(S): Zhang, Bei B.; Moller, David E.

CORPORATE SOURCE: Merck Research Laboratories, Department of Molecular Endocrinology, Rahway, NJ, 07065, USA

SOURCE: Current Opinion in Chemical Biology (2000), 4(4), 461-467
CODEN: COCBF4; ISSN: 1367-5931

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review with 50 refs. Type 2 diabetes is a chronic metabolic derangement that results from defects in both insulin action and secretion. New thiazolidinedione insulin sensitizers have been recently launched. New approaches with mechanisms different from current therapies are being explored, including novel ligands of peroxisome proliferator-activated receptor, glucagon receptor antagonists, dipeptidyl peptidase IV inhibitors, and insulin receptor activators.

REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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(FILE 'HOME' ENTERED AT 07:30:40 ON 09 MAY 2007)

FILE 'CAPLUS' ENTERED AT 07:30:52 ON 09 MAY 2007
L1 2176 S DIPEPTIDYL PEPTIDASE IV
L2 1037 S L1 AND INHIBITOR?
L3 541 S L2 AND DIABETES
L4 45 S L3 AND PY<2002

FILE 'STNGUIDE' ENTERED AT 07:33:06 ON 09 MAY 2007

FILE 'CAPLUS' ENTERED AT 07:35:04 ON 09 MAY 2007

FILE 'STNGUIDE' ENTERED AT 07:35:12 ON 09 MAY 2007

FILE 'CAPLUS' ENTERED AT 07:35:41 ON 09 MAY 2007

FILE 'STNGUIDE' ENTERED AT 07:35:41 ON 09 MAY 2007

=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.06	116.79

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL

	ENTRY	SESSION
CA SUBSCRIBER PRICE	0.00	-31.20

STN INTERNATIONAL LOGOFF AT 07:36:27 ON 09 MAY 2007